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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,978	09/15/2006	David I. Cohen	51311-00009	2811

45200 7590 03/25/2009

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EXAMINER	
SNYDER, STUART	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
03/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,978	COHEN, DAVID I.	
	Examiner	Art Unit	
	STUART W. SNYDER	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/20/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of the species HIV tat in the reply filed on 11/20/2008 is acknowledged. Claims 1-5 are pending and examined herein.

Specification

2. The Specification is objected to because the "Brief Description of the Drawing" (see page 8, paragraphs 0032-0034) refers to "signal transduction", "cysteine-rich", and "membrane translocation" domains or sequence apparently referring to the "hatched" portion of Figures 10-12, respectively, but without specific reference to these portions of the drawings. Literal reference to the "hatched" elements of the drawings in the Specification may obviate this objection although care must be made not to add new matter.

3. The Specification is objected to because the "Brief Description of the Drawing" (see page 9, paragraph 0038) references Figure 16. However, there are two panels of Figure 16, 16A and 16B. Literal reference to Figures 16A and 16B as Applicants have done for Figure 9 may obviate this objection although care must be made not to add new matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap

between the steps. See MPEP § 2172.01. The omitted steps are: A step in at least claim 1 that relates the purpose of the method recited in the preamble, "identifying new immunomodulatory chemical entities", to a result necessary for a skilled artisan to conclude that the artisan has identified such an entity. Such steps are often formulated as "wherein" clauses; for example, "wherein determining the presence of DCs or ARegs identifies a NICE".

Claims 2-5 depend directly or indirectly on claim 1 and are therefore also incomplete for omitting an essential step.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen (US Pat. 6,667,151) in view of Cohen, *et al*, Cheadle, *et al*. and Baghian, *et al*. The claims are drawn to a method of identifying novel immunomodulatory chemical entities (NICE) and including the steps of: Reacting candidate novel immunomodulatory chemical entities (cNICE) with a solid phase Tat SH3, identifying candidates that bind to solid phase Tat SH3, adding identified cNICEs to cultured PBMCs, adding Tat to cNICE/PBMC cultures and further incubating said Tat/cNICE/PBMC cultures to allow differentiation of PBMCs into DCs or ARegs and determining the presence of DCs or ARegs (Claim 1). Claims 2-5 add

the following limitations: The Tat SH3 binding domain is selected from various Tat species, especially including elected HIV Tat (claim 2); an additional step of injecting an identified NICE into an immunosuppressed mouse wherein immunosuppression of the mouse results from the presence of an endogenous SH3 binding domain (claim 3) especially a hairless mouse (claim 4); and sequentially injecting a mouse with a "tolerogenic" NICE followed by an antigen that would evoke an immune response in said mouse without pre-injection of said "tolerogenic" NICE.

Cohen is considered as the closest prior art document discloses an *in vitro* method to test for the immunomodulatory properties of tat (column 11, second paragraph to last paragraph of column 12) in cultured macrophages obtained from peripheral blood. An *in vivo* method is further disclosed on column 11, first paragraph comprising the injection of tat in a mouse and challenging the mouse with an immunogen to evaluate tolerance to that antigen. The same teaching can be derived from Cohen, *et al.* see Table 1, Figure 1 and page 10843. The difference between Cohen or Cohen *et al.* and the present application is the provision of a screening method combined with an *in vitro* testing method. The problem is therefore seen as the provision of a method of screening for other drugs having properties similar to tat, in particular the tolerogenic property linked to the SH3 domain of tat of HIV-1.

Cheadle, *et al.* discloses a screening method using SH3 domains (see Abstract, Materials and Methods, and Results sections) involving phage display wherein

candidate phages were screened for their ability to bind to immobilized SH3 domains. Cohen and Cohen, *et al.* disclose various test methods to evaluate the tolerogenic potential of different tat proteins of the prior art.

With regard to the subject-matter of claims 3-5, Cohen and Cohen, *et al.* already disclose an *in vivo* testing method of tat in mice that comprises the step of injecting tat and challenging the mouse with an antigen. The only difference is the use of an immunosuppressed mouse in particular a hairless mouse. These mice are known (Baghian, *et al.*) and the use of these mice rather than conventional mice does not render the subject-matter of claims 3-5 non-obvious.

A skilled artisan would have found it obvious to combine the cited references to arrive at a method of identifying NICEs. The skilled artisan would have been motivated to include the method of Cheadle, *et al.* for generating cNICEs because of the ease of generating such candidates by phage display (see introduction); include the method of Cohen or Cohen, *et al.* to limit SH3 binding cNICEs to those that have biological activity (see, introductions); and use of hairless mice taught by Baghian, *et al.* The skilled artisan would have a reasonable expectation of success in identifying and characterizing NICE because of the robustness of each independent method and the knowledge that cNICEs identified by binding methods are further validated as having *in vitro* and *in vivo* biological activity as taught by Cheadle, *et al.* Thus, the instantly claimed method of identifying NICEs as a whole is prima facie obvious over Cohen, Cohen, *et al.*, Cheadle, *et al.* and Baghian, *et al.*

Conclusion

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STUART W. SNYDER whose telephone number is (571)272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

   Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
Primary Examiner, Art Unit 1648

Stuart W Snyder
Examiner
Art Unit 1648

sws